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Case report

Nicorandil-induced penile ulcerations: A case report and review of the penile cutaneous circulation

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ABSTRACT

Mucosal and cutaneous ulceration as a result of nicorandil use is well described in the literature. Nicorandil induced penile ulceration is a rare clinical manifestation. Six cases arising from either the dorsal or lateral prepuce have been reported in current literature. We present a case of nicorandil induced penile ulceration affecting the dorsolateral prepuce and give an overview of the penile cutaneous circulation.

Introduction

Penile ulceration in elderly patients is usually secondary to infections and malignancy.[1] Since its introduction to Europe in 1994 for medical prophylaxis of angina, a number of reports have implicated nicorandil as a cause of both mucosal and cutaneous ulceration.[2] To date, the literature contains six cases of nicorandil induced penile skin ulceration.[1,3,4] All reports describe ulceration of the dorsal or lateral penile skin. Here we report a patient with a dorsolateral penile cutaneous fistula assumed to be caused by nicorandil use. In addition, we also review the penile cutaneous blood supply and postulate the reasons for the location of the ulceration.

Case report

A 70 year old gentleman was referred with a 12 month history of painless penile ulceration located over the dorsolateral penile skin. His past medical history included ischemic heart disease with

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associated coronary artery stenting, type II diabetes and hypertension, for which he took nicorandil 20 mg twice daily for 24 months. He was an ex-smoker with an unremarkable urological or genito-urinary medicine history. Examination revealed a 30 mm well circumscribed, cutaneous fistula over the distal one-third of the dorsolateral penile skin with protrusion and tethering of the glans (Figure 1). There was no associated inguinal lymphadenopathy. He subsequently underwent ulcer excision and refashioning of the existing penile skin to recreate the appearance of a circumcised penis (Figures 2 and 3). No samples were sent for histological assessment. At 2 months post operatively, the patient reported tightness over the dorsum of his penis during erections. He was advised to stretch the dorsal skin. At 8 months post op this problem had resolved and the patient was discharged.

Discussion

Numerous causes of spontaneous penile ulceration have been described.[1,5,6] In the younger patient sexually transmitted pathologies such as primary syphilis, lymphogranuloma venereum and granuloma inguinale are a common cause.[5] In addition, certain granulomatous disorders including Crohn's disease, Bechet's disease and pyoderma gangrenosum can also cause ulceration to the genitals of younger patients.[5] However, in the elderly, penile ulceration is usually attributed to the side effects of certain medications, specifically Nicorandil or Foscarnet, urinary tract infections or malignancies.[1,6] In our case, the patient did not have any known reported risk factor for spontaneous penile ulceration other than regular nicorandil use, and as such it was assumed as the likely cause.

Nicorandil is a nicotinamide ester which through dual pharmacodynamics reduces both the cardiac preload and afterload and increases coronary blood flow.[1,7,8] These actions are achieved by activation of guanylyl cyclase through its nitrate moiety and by its agonistic effect on ATP sensitive potassium channels located on peripheral and coronary arterioles. Most of its adverse reactions are linked to these properties and include flushing and headache. In addition, numerous reports have implicated nicorandil as a reversible cause of oral and anal mucus membrane ulceration.[8] More recently, the literature describes cases of cutaneous ulceration of parastomal and penile skin.[1,3,4,9] Two main theories exist regarding the physiopathogenesis of nicorandil induced ulceration, these include a vascular steal phenomenon and direct local toxic effect from its metabolite.[1] Embryologically, the prepuce does not form in situ but arises from a combination of folding and unfolding over a mesodermal core along with epithelial ingrowth and proliferation from the coronal margin near the glans.[10] Initially, it has a single terminal arterial system in the mesenchyme that ends at the preputial ring supplying the inner and outer preputial surfaces. With development, the arterial input is through four branches from the inferior external pudendal arteries. Two branches enter the superficial penile fascia dorsolaterally whilst the other two enter it ventrolaterally. After birth, these four superficial penile arteries supply

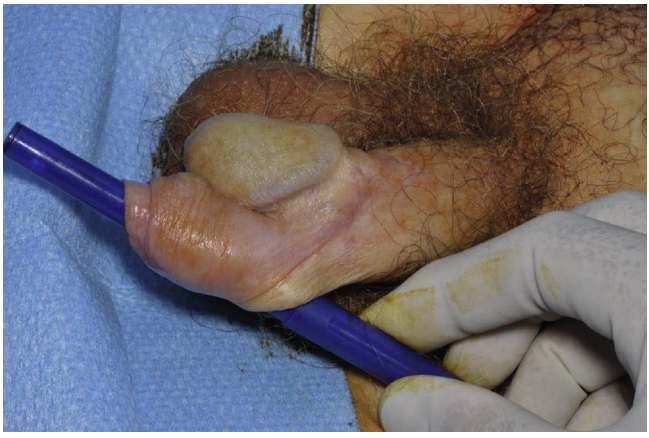

Figure 1. Dorsolateral penile cutaneous fistula.

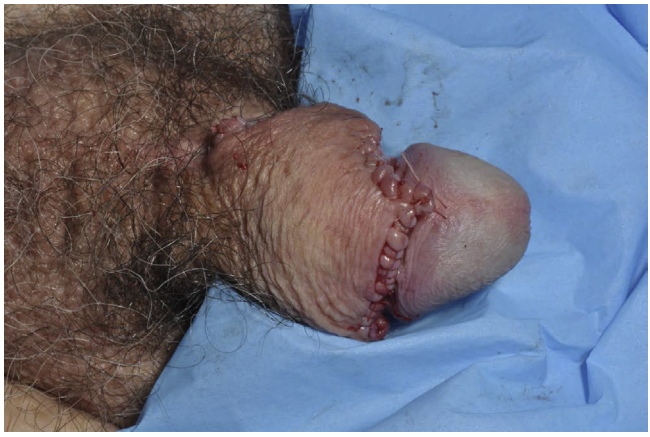

Figure 2. Post operative images showing excision of the cutaneous fistula with circumcision reconstruction.

Figure 3. Post operative images showing excision of the cutaneous fistula with circumcision reconstruction.

both the outer and inner preputial surfaces in continuity and for this reason the two surfaces are considered as a single unit.[11] We hypothesize that ulceration occurs on the dorsal or lateral surface because its blood supply relies solely on this single unit. Unlike the dorsal and lateral surfaces, the ventral surface has added collateral supply from the dorsal artery of the penis which gives off branches to the frenulum.

With regards to management of nicorandil induced mucosal ulcers it has been well documented that healing occurs with drug cessation.[3] Different management options for nicorandil induced penile ulcers have been described which include combined circumcision and drug cessation and drug cessation only. For the four patients managed with combined circumcision and discontinuation of nicorandil, healing was quicker than the two with discontinuation of nicorandil.[1,3,4] We suggest that patients should be managed with combined circumcision and drug cessation.

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